UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/757,716	01/09/2001	Holly Magna	PF-0420-2 DIV	8687

22428 7590 07/14/2004

FOLEY AND LARDNER
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
VANDERVEGT, FRANCOIS P	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/757,716	MAGNA ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-49,51,53-62 and 65-68* is/are pending in the application.

4a) Of the above claim(s) *61 and 62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-49,51,53-62 and 65-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation of U.S. Application Serial Number 09/153,586, which claims the benefit of the filing date of provisional applications 60/064,552 and 60/046,555.

Claims 1-44, 50, 52, 63 and 64 have been canceled.

Claims 45, 61 and 63 stand as withdrawn pursuant to Applicant's election with traverse in the paper filed June 23, 2002.

Claims 45-49, 51, 53-62 and 65-68 are currently pending.

Claims 45, 47, 61 and 62 stand as withdrawn pursuant to Applicant's election with traverse in the paper filed June 23, 2002.

Claims 46, 48, 49, 51, 53-60 and 65-68 are the subject of examination in the present Office Action.

1. In view of Applicant's arguments filed April 8, 2004, **the following grounds of rejection are maintained**.

2. The **declarations of Rockett, Bedilion and Iyer filed April 8, 2004 have not been considered** because they do not speak specifically to the application being examined but are merely generic statements providing the views of the declarants regarding microarrays and toxicology testing in general. None of the declarations specifically deal with the utlity, enablement, novelty or non-obviousness of the claimed antibody or of the polypeptide of SEQ ID NO: 1 to which the antibody is directed.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 46, 48, 49, 51, 53-60 and 65-68 stand rejected under 35 U.S.C. 101 because the claimed invention lacks a credible asserted utility or a well-established utility.

It was previously stated: "The claims are most broadly drawn to a antibodies directed to "a) a polypeptide having the amino acid sequence of SEQ ID NO: 1, b) a polypeptide having a naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, wherein the polypeptide has nucleotide pyrophosphohydrolase activity, c) a fragment of a polypeptide

having the amino acid sequence of SEQ ID NO:1, wherein the fragment has nucleotide pyrophosphohydrolase activity, and d) an immunogenic fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1." Claims are also drawn to the making of antibodies using the sequences [claims 53 and 56] and methods of diagnosis using the antibodies [claim 47].

The polypeptide of SEQ ID NO: 1 and naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 1 to which the claimed antibodies are directed are not supported by either a specific and substantial asserted utility or a well-established utility. While the specification asserts that the utility of the polypeptides is for "the diagnosis, prevention and treatment of arthropathies, immunological disorders and cancers" (page 3, lines 10-13 for example), in order to establish such an asserted utility as substantial or well-established, there must be credible evidence that the polypeptide is of consequence in the conditions being diagnosed or treated. A well established utility is a specific, substantial, and credible utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material. Identifying a DNA segment derived from overlapping cDNAs and determining a function for it's deduced putative polypeptide product based solely on primary polypeptide sequence does not endow the polypeptide with such a utility. Applicant has generated the deduced amino acid sequence of the protein product (SEQ ID NO:1) from a consensus nucleic acid sequence generated via computer alignments using the partial cDNA sequence of Masuda et al (8 on form PTO-1449) and a computer homology search of cDNAs from an osteoarthritic chondrocyte cDNA library. SEQ ID NO: 1 was derived from cDNA sequences of three clones from the same cDNA library (page 15, line 26 to page 16, line 10 of the instant specification, for example). Applicant has disclosed this deduced amino acid sequence is a nucleotide pyrophosphohydrolase protein termed by Applicant as NTPPH-2 and has disclosed that this computer generated molecule polypeptide has 50% amino acid identity in a computer generated sequence alignment with the known porcine nucleotide pyrophosphohydrolase disclosed by Masuda et al (8 on form PTO-1449) and Cardenal et al (7 on form PTO-1449) as NTPPH; instantly referred to by the specification as NTPPH-1 (page 2, lines 16 to page 3, line 9 and page 16, lines 16-17 for example). The specification states purported uses for the protein including "the diagnosis, prevention and treatment of arthropathies, immunological disorders and cancers" (page 3, lines 10-13 for example). However, there is no clear guidance from the specification that their protein would have the same or similar biological properties as NTPPH because the proposed uses for the claimed computer deduced protein are based solely upon computer alignment with known proteins and the site of isolation, osteoarthritic chondrocytes, of the cDNA sequences from which the amino acid sequence was deduced. Since the claimed protein and the prior art proteins only share 50% sequence identity there would be no predictability that this small sequence identity would render the biological activities of the proposed protein and the known porcine nucleotide pyrophosphohydrolase similar because Applicant has not disclosed whether the biological activity of both proteins resides within the common region(s) or elsewhere within the sequence of the proteins, nor does the specification indicate whether the proteins share conserved active or binding sites. Brenner et al. (Proc. Natl. Acad. Sci. USA (1998) 95:6073-6078; U1 on form PTO-892), at page 6076, column 2, states that, "Fig. 2 shows one of the many pairs of proteins with very different structures that nonetheless have high levels of identity over considerable aligned regions. Despite the high identity, the raw and the statistical scores for such incorrect matches are typically not significant. The principal reasons percentage identity does so poorly seems to be that it ignores information about gaps and about the conservative or radical nature of residue substitutions. From the PDB90D-B analysis in Fig. 3, we learn that 30% identity is a reliable threshold for this database only for sequence alignments of at least 150 residues." Brenner therefore shows in Fig. 2 that reliance upon high identity alone in many pair wise comparisons is insufficient to relate information about structural and/or functional relatedness and in the analysis of Fig. 3 indicates that information which can be gleaned from sequence identity comparisons is database-specific, not general. The Brenner reference puts further emphasis on the need for structural relationships on page 6074, end of first column

in the statement, "Since the discovery that the structures of hemoglobin and myoglobin are very similar though their sequences are not, it has been apparent that comparing structures is a more powerful (if less convenient) way to recognize distant evolutionary relationships than comparing sequences." Therefore, the Brenner reference teaches that sequence identity alone is insufficient to establish functional relationships between proteins, rather it must be used in concert with structural information to accurately establish relationships between proteins. The instant specification does not provide any information on the structural characteristics of NTPPH-2, only an assertion of 3 putative N-glycosylation sites and 25 putative phosphorylation sites and that "NTPPH-2 has chemical and structural homology with NTPPH-1" (page 16, lines 11-17 for example), but this "structural homology" is based solely on the finding of 50% homology to NTPPH, and not actual structural determination. According to Brenner, sequence homology must be used in concert with structural information, rather than using one to guess the other. The instant specification does not provide any information about the structure of the predicted NTPPH-2 polypeptide, only sequence identity to the porcine nucleotide pyrophosphohydrolase NTPPH, and for this reason the specification provides insufficient information to enable the artisan to reasonably predict that NTPPH-2 is functionally related to NTPPH and therefore the specification does not teach the artisan a credible utility for NTPPH-2.

Because the characteristics of NTPPH-2 are based solely upon sequence identity of the protein with other previously known proteins and not based upon analysis of any actually-produced protein product, no biological activity has been established for NTPPH-2. As such, further research would be required to identify or reasonably confirm a "real world" context of use, for example, to identify any function of NTPPH-2 and conditions for which NTPPH-2 polypeptides, fragments and "naturally occurring" 90% identical polypeptides would be of diagnostic or therapeutic significance. Accordingly, without a "real-world" use for the protein, antibodies specific therefore are equally not useful, as basic research such as studying the properties of the product of the polypeptide are not considered substantial and credible utility for the claimed invention. Therefore, the specification does not fairly disclose a substantial and credible utility for the antibody of the instant claims. See Brenner v. Manson, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966), noting "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." A patent is therefore not a license to experiment. Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001."

Applicant's arguments filed April 8, 2004 have been fully considered but they are not persuasive. Applicant argues that the claimed antibodies,

> "have specific, substantial and credible utilities in, for example, the purification and/or detection of polypeptides. It is the polypeptides which are the object of further research, not the claimed antibodies. In these methods, the claimed antibodies are tools which facilitate research on the peptides. For example, purification of polypeptides using the claimed antibodies has the useful benefit of providing the polypeptides in a form suitable for further research on the polypeptides."

Applicant's arguments are circular in nature, asserting essentially that "the polypeptide is the compound of interest, but needs more study so we will isolate antibodies to the polypeptide, so that we can isolate more polypeptide and study it further." Contrary to Applicant's position, the asserted method of use does not establish a specific, substantial and credible utility for the claimed antibody in accordance

with the Utility Guidelines, as set forth in MPEP 2107.01. In regard to a specific utility, the guidelines state that:

> A "specific utility" is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. Office personnel should distinguish between situations where an applicant has disclosed a specific use for or application of the invention and situations where the applicant merely indicates that the invention may prove useful without identifying with specificity why it is considered useful. For example, indicating that a compound may be useful in treating unspecified disorders, or that the compound has "useful biological" properties, would not be sufficient to define a specific utility for the compound. Similarly, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target. A general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed. Contrast the situation where an applicant discloses a specific biological activity and reasonably correlates that activity to a disease condition. Assertions falling within the latter category are sufficient to identify a specific utility for the invention. Assertions that fall in the former category are insufficient to define a specific utility for the invention, especially if the assertion takes the form of a general statement that makes it clear that a "useful" invention may arise from what has been disclosed by the applicant. Knapp v. Anderson, 477 F.2d 588, 177 USPQ 688 (CCPA 1973).

In the instant case, Applicant has identified that a "useful biological property" of the claimed antibody is to bind the disclosed polypeptide to isolate the polypeptide for further study. However, in accordance with the guidelines, Applicant's assertions are insufficient to define a specific utility for the invention because the statement makes it clear that a "useful" invention (further characterization of the NTPPH-2 polypeptide) may arise from what has been disclosed by Applicant (antibodies to a polypeptide that has been deduced from a nucleic acid sequence identified as NTPPH-2 solely on sequence homology to a known protein and without any real knowledge of the biological properties of NTPPH-2.

In regard to a substantial utility, the guidelines state that:

> A "substantial utility" defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":
> (A) Basic research such as studying the properties of the claimed product itself or

the mechanisms in which the material is involved;
(B) A method of treating an unspecified disease or condition;
(C) A method of assaying for or identifying a material that itself has no specific and/or substantial utility;
(D) A method of making a material that itself has no specific, substantial, and credible utility; and
(E) A claim to an intermediate product for use in making a final product that has no specific, substantial and credible utility.
Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations in other cases to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. See, e.g., Brenner v. Manson, 383 U.S. 519, 534-35, 148 USPQ 689, 695 (1966). Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a "substantial" utility.

In the instant case, Applicant has identified that the claimed antibody is "useful" for further research of the polypeptide (pages 7-8 of response, for example). Applicant further asserts that it is improper for the Office to base the instant rejection on the lack of utility of the recited polypeptide because the claims are drawn to the antibody, not the polypeptide. However, in accordance with the guidelines as set forth above, the claimed antibody does not have a "real world" context of use because, since the actual function of the target polypeptide is not known, use of the antibody for further research such as studying the properties of the disclosed polypeptide can only constitute "basic research" of the recited polypeptide.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 46, 48, 49, 51, 53-60 and 65-68 also stand rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

It was previously stated: "Additionally, even in view of a testable activity for those polypeptides that are "naturally-occurring" variants of SEQ ID NO:1 comprising at least 90% identity over the full length of SEQ ID NO:3, the specification still does not appear to provide sufficient guidance such that the skilled artisan is enabled to make and use an antibody to those polypeptides commensurate in scope with the instant claims.

The specification discloses a single working example of a polypeptide that is naturally-occurring and has at least 90% identity to SEQ ID NO: 1; namely, the polypeptide of SEQ ID NO: 1. Nevertheless, there is insufficient guidance in the specification as-filed to direct a person of skill in the art as to how to make and use antibodies to a polypeptide comprising a "naturally-occurring" amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 1 even wherein said naturally-occurring amino acid sequence has nucleotide pyrophosphohydrolase activity.

Applicant does not appear to have provided sufficient guidance with respect to "naturally-occurring" polypeptides and how to make and use antibodies to them. Although the specification does provide some general guidance as to how to isolate other nucleic acids related to the nucleic acid encoding SEQ ID NO: 1 and then test those polypeptides encoded by the related nucleic acids for nucleotide pyrophosphohydrolase function (e.g., page 55), it is unpredictable that other "naturally-occurring" polypeptides having nucleotide pyrophosphohydrolase activity and at least 90% amino acid sequence identity to SEQ ID NO: 1 exist.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Applicant does not appear to provide sufficient guidance as to other sources of "naturally-occurring" polypeptides which are at least 90% identical to SEQ ID NO: 1 and have nucleotide pyrophosphohydrolase activity. The state of the art did not recognize other "naturally-occurring" polypeptides that had nucleotide pyrophosphohydrolase activity and were at least 90% identical to SEQ ID NO: 1. Even though the level of skill in the art for isolating "naturally-occurring" polypeptides encoded by nucleic acids related to the nucleic acid encoding SEQ ID NO: 1 may have been high with respect to the techniques employed, skill in the art does not render the existence of a "naturally-occurring" polypeptide predictable.

The presence of a single working example and the failure of the state of the art either at the time of filing or since to recognize other "naturally-occurring" polypeptides at least 90% identical to SEQ ID NO: 1 and having nucleotide pyrophosphohydrolase activity indicates that it was highly unpredictable that additional polypeptides meeting these limitation could be isolated, particularly based on the limited guidance provided in the specification as filed. Unlike the fact pattern of In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) where the presence of a hybridoma producing an antibody having the desired properties among the many hybridomas was predictable, in the instant case it is not predictable that other "naturally-occurring" polypeptides exist. Therefore, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue with respect to other "naturally-occurring" polypeptides other than SEQ ID NO: 1.

Consequently, a person of skill in the art is not enabled to make and use an antibody to a "naturally-occurring" polypeptide at least 90% identical to SEQ ID NO: 1 and having nucleotide pyrophosphohydrolase activity; as encompassed by the full breadth of the claims as currently recited, irrespective of the particular form of the antibody (polyclonal, monoclonal, etc.)."

Applicant argues that the specification is fully enabling for the making of antibodies commensurate with the scope of the claims because the specification "discloses methods methods to make antibodies which specifically bind to a polypeptide having **any** particular amino acid sequence" (page 16 of response, emphasis in original) and thus "one of skill in the art would be able to routinely obtain antibodies which specifically bind to any of the recited variants and fragments of SEQ ID NO: 1." Applicant asserts that they need only disclose information sufficient to permit one of ordinary skill in the art to make and use the invention as claimed, without undue experimentation. However, with SEQ ID NO: 1 being a polypeptide of 1156 amino acid residues, "variants" that are "at least 90% identical"

encompasses polypeptides with up to at least 115 undisclosed amino acid residues, resulting in a genus of at least 115^{20} or 1.64×10^{41} different polypeptide variants. Disclosure of a single amino acid sequence (SEQ ID NO: 1) is not sufficient to enable the making of antibody to all these variants, because many of these "naturally-occurring variants" will comprise immunological epitopes not found in the single disclosed species of SEQ ID NO: 1. The Court held that, "It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement" (Genentech Inc. v. Novo Nordisk A/S 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997)). While a specification does not need to disclose what is well known in the art, that rule does not excuse Applicant from providing a complete disclosure. In the instant case, while the artisan may be able to make antibodies to a given polypeptide sequence, disclosure of a single species of a genus of over 1.64×10^{41} different polypeptide variants can hardly be considered complete and the enablement requirement has therefore not been met.

5. Claims 46, 48, 49, 51, 53-60 and 65-68 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It was previously stated: "The claims recite as part of the invention an antibody which specifically binds a polypeptide comprising a "naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 1" wherein said naturally-occurring amino acid sequence has nucleotide pyrophosphohydrolase activity.

A polypeptide comprising the amino acid sequence of SEQ ID NO:1 is adequately described in the specification as-filed, thereby providing an adequate written description of an antibody which specifically binds the polypeptide of SEQ ID NO:1 or immunogenic fragments thereof.

A polypeptide comprising a "naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1" wherein said naturally-occurring amino acid sequence has nucleotide pyrophosphohydrolase activity is a recitation of a genus of polypeptides for which Applicant has disclosed a single species: the polypeptide of SEQ ID NO:1. The claim recites that the polypeptide to which the antibody binds is "naturally-occurring" and has a testable function of "nucleotide pyrophosphohydrolase activity." The specification proposes that other members of the "naturally-occurring" polypeptide genus may be identified by using hybridization probes to identify DNAs or RNAs related to the nucleic acid encoding SEQ ID NO:1, expressing the polypeptide, and assaying the polypeptide for nucleotide pyrophosphohydrolase activity (see page 39 and page 55 in particular).

However, Applicant does not appear to have provided a description of which polypeptide sequences are "naturally-occurring", even among those polypeptides at least 90% identical to the full length of the sequence of SEQ ID NO: 1. Neither does Applicant appear to have provided a description of how the structure of the polypeptide of SEQ ID NO:3 relates to the structure of other "naturally-occuring" polypeptides which have nucleotide pyrophosphohydrolase activity, even for those polypeptides at least 90% identical to the full length of the sequence of SEQ ID NO: 1. Thus neither the

common attributes of the genus nor the identifying attributes of individual species other than SEQ ID NO: 1 appear to have been described.

One of skill in the art would conclude that Applicant was not in possession of the claimed genus of polypeptides comprising a "naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1" wherein said naturally-occurring amino acid sequence has nucleotide pyrophosphohydrolase activity. Since Applicant does not appear to have been in possession of the genus of polypeptides to which the instantly recited antibody specifically binds; Applicant in turn does not appear to be in possession of the genus of antibodies specifically binding these polypeptides.

Therefore, only an antibody to SEQ ID NO: 1 or immunogenic fragments thereof meet the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398."

Applicant argues that the specification contains an adequate written description of the claimed invention because the specification teaches SEQ ID NO: 1 and methods by which variants that are "at least 90% identical" and having pyrophosphohydrolase activity can be identified (page 21 of response). Applicant further asserts that because the claims are directed to the antibodies, not proteins, "it is the properties of the antibodies, not the proteins they bind, which is relevant" (page 22 of response). In this Applicant is correct. However, since Applicant has only described a single protein, SEQ ID NO: 1, out of a genus of over 1.64×10^{41} different polypeptide variants that the claimed antibody can bind to. Therefore, Applicant has only demonstrated possession of antibodies that specifically bind to SEQ ID NO: 1. While these antibodies that specifically bind to SEQ ID NO: may also specifically bind to naturally-occurring variants that are 90% identical to SEQ ID NO: 1 and has pyrophosphohydrolase activity, Applicant has not demonstrated possession of antibodies that specifically bind to naturally-occurring variants that are 90% identical to SEQ ID NO: 1 and has pyrophosphohydrolase activity but DO NOT also bind SEQ ID NO: 1. Accordingly, the specification does not provide an adequate written description of the claimed genus of antibodies.

Conclusion

6. No claim is allowed.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
June 28, 2004

PATRICK J. NOLAN, PH.D.
PRIMARY EXAMINER
6/28/04